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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/031,546	01/18/2002	Gregory A. Demopulos	OMER118473	6615

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EXAMINER	
YOUNG, MICAH PAUL	
ART UNIT	**PAPER NUMBER**
1618	

MAIL DATE	DELIVERY MODE
09/23/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/031,546	DEMOPULOS ET AL.	
	Examiner	Art Unit	
	MICAH-PAUL YOUNG	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 May 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38,39,44-51,53,60,73-76 and 81* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38,39,44-51,53,60,73-76 and 81* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/24/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgment of Papers Received: Amendment/Response dated 5/23/08.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

1. Claims 38, 39, 44-51, 53, 73-76, and 81 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined disclosures of Pelletier et al (UPSN 5,972,880 hereafter '880) in view of Hunziker (USPN 5,206,023 hereafter '023). The claims are drawn to method of inhibiting cartilage degradation in a joint comprising delivering to the joint a composition comprising two chondroprotective agents.

2. The '880 patent discloses a method of treating osteoarthritis comprising the administration of compounds that inhibit cartilage catabolism (abstract). The compounds include interleukin receptor antagonist (examples). The method of treatment includes an intra-articular

injection of an interleukin 1 receptor antagonist (col. 3, lin. 5-20). The reference also establishes the connection between the biological effects of IL-1 and those of transforming growth factors beta. The IL-1 has been shown to modulate the effect of TGF beta on the body (col. 4, lin. 1-20). Though not explicitly disclosed, it can be seen that the compounds have a synergistic effect, regulating and modulating each other. Inhibiting IL-1 effects decrease tissue growth and the effects of TGF-beta.

3. The '023 patent teaches methods for the treatment and repair of defects of lesions in cartilage (abstract). The method includes the delivery via injection a composition comprising anabolic promoting compounds such as fibroblast growth factors, transforming growth factor betas (3,4,5 etc), insulin growth factor-4 (col. 4, lin. 49-64; col. 5, lin. 44-58, example 3; claims) and chemotactic agents such as tumor necrosis factors (col. 7, lin. 50-65). The growth factors are combined with other components in methods to treat defects in knee cartilage (examples). The concentrations of the injection can be modulated to fit the needs of the patient (example)

4. Since both '880 and '023 disclose compositions for the treatment of cartilage damage, it would be well within the level of skill in the art to combine them in order to provide an improved cartilage treatment composition. It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose. The idea of combining them flows logically from their having been individually taught in the prior art. *See* In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). The combination of the interleukin –1 receptor antagonist with the anabolic compounds of '023 would modulate each other, and work toward a mutual cartilage preserving need.

5. With these things in mind one of ordinary skill in the art would recognize how the IL-receptor antagonist of the '880 would help modulate the effects of the growth factors of the '023 patent allowing them to increase production of proteoglycans without over producing and creating osteophytes causing osteoarthritis. The interleukin antagonist compounds would keep the growth factors in check while they promoted anabolic growth in the damaged cartilage. This combination would be obvious since an over growth of osteophytes is recognized as a contributor to osteoarthritis. This combination would have been obvious to one of ordinary skill in the art with an expected result of a regulating injection compound able to treat damaged cartilage while avoiding osteoarthritis.

Response to Arguments

Applicant's arguments filed 5/18/08 have been fully considered but they are not persuasive. Applicant argues that:

> The patent references teach away from each other and therefore there is no motivation to combine the patents.

Regarding this argument it is the position of the Examiner that the combination of the '880 and '023 patent continue to obviate the claims. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In the instant case the '880 patent discloses a method of treating osteoarthritis with interleukin receptor antagonist. These IL antagonists are effective for reducing the progression of lesions and cartilage degradation. These antagonists are also thought to modulate

growth factor activity related to the formation of osteophytes formation. The antagonists were effective in reducing the size of lesions on tibial plateaus (col. 9, lin. 30-45). The effects are dose specific, increasing with an increase in dosage. With this in mind it would have been obvious to include compounds that also show activity in lesion size reduction. It would have been obvious to include a further compound that would also reduce the size of said lesion. The '023 patent discloses method of treating lesion and degradation of articular cartilage by administering various growth factors, including Transforming Growth Factor Beta. TGF beat is shown in reducing lesion size by activating repair cells to the lesion site and effectively closing the lesion site (example 4). It would have been obvious to combine these compounds since they perform the same function to the same end. Applicant has argues that the prior art teaches away from each other, however the '880 patent does not teach away from the use of growth factors, only suggesting that excessive growth factors might play a role in osteophytes formation, suggesting that modulation would be in order. The idea of combining them flows logically from their having been individually taught in the prior art. *See* In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). For these reason the claims remain rejected.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICAH-PAUL YOUNG whose telephone number is (571)272-0608. The examiner can normally be reached on Monday-Friday 7:00-4:30; every other Monday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

/MICAH-PAUL YOUNG/
Examiner, Art Unit 1618